WHAT IS CLAIMED IS

1. A method for sterilizing one or more tissues that are sensitive to radiation, said method comprising irradiating said one or more tissues with radiation for a time effective to sterilize said one or more tissues at a rate effective to sterilize said one or more tissues and to protect said one or more tissues from said radiation.

2. A method for sterilizing one or more tissues that are sensitive to radiation, said method comprising:

(i) applying to said one or more tissues at least one stabilizing process selected from the group consisting of:

(a) adding to said one or more tissues at least one stabilizer in an amount effective to protect said one or more tissues from said radiation;

(b) reducing the residual solvent content of said one or more tissues to a level effective to protect said one or more tissues from said radiation;

(c) reducing the temperature of said one or more tissues to a level effective to protect said one or more tissues from said radiation;

(d) reducing the oxygen content of said one or more tissues to a level effective to protect said one or more tissues from said radiation;

(e) adjusting or maintaining the pH of said one or more tissues to a level effective to protect said one or more tissues from said radiation; and

(f) adding to said one or more tissues at least one non-aqueous solvent in an amount effective to protect said one or more tissues from said radiation;

and

(ii) irradiating said one or more tissues with a suitable radiation at an effective rate for a time effective to sterilize said one or more tissues.

3. A method for sterilizing one or more tissues that are sensitive to radiation, said method comprising:

(i) applying to said one or more tissues at least one stabilizing process selected from the group consisting of:

(a) adding to said one or more tissues at least one stabilizer;

(b) reducing the residual solvent content of said one or more tissues;

(c) reducing the temperature of said one or more tissues;

(d) reducing the oxygen content of said one or more tissues;

(e) adjusting or maintaining the pH of said one or more tissues; and

(f) adding to said one or more tissues at least one non-aqueous solvent;

and

(ii) irradiating said one or more tissues with a suitable radiation at an effective rate for a time effective to sterilize said one or more tissues, wherein said at least one stabilizing process and the rate of irradiation are together effective to protect said one or more tissues from said radiation.

4. A method for sterilizing one or more tissues that are sensitive to radiation, said method comprising:

(i) applying to said one or more tissues at least two stabilizing processes selected from the group consisting of:

(a) adding to said one or more tissues at least one stabilizer;

(b) reducing the residual solvent content of said one or more tissues;

(c) reducing the temperature of said one or more tissues;

(d) reducing the oxygen content of said one or more tissues;

(e) adjusting or maintaining the pH of said one or more tissues; and

(f) adding to said one or more tissues at least one non-aqueous solvent;

and

(ii) irradiating said one or more tissues with a suitable radiation at an effective rate for a time effective to sterilize said one or more tissues, wherein said at least two stabilizing processes are together effective to protect said one or more tissues from said radiation and further wherein said at least two stabilizing processes may be performed in any order.

5. The method according to claim 2, 3 or 4, wherein said residual solvent is an organic solvent.

6. The method according to claim 1, 2, 3 or 4, wherein said effective rate is not more than about 3.0 kGy/hour.

7. The method according to claim 1, 2, 3 or 4, wherein said effective rate is not more than about 2.0 kGy/hr.

8. The method according to claim 1, 2, 3 or 4, wherein said effective rate is not more than about 1.0 kGy/hr.

9. The method according to claim 1, 2, 3 or 4, wherein said effective rate is not more than about 0.3 kGy/hr.

10. The method according to claim 1, 2, 3 or 4, wherein said effective rate is more than about 3.0 kGy/hour.

11. The method according to claim 1, 2, 3 or 4, wherein said effective rate is at least about 6.0 kGy/hour.

12. The method according to claim 1, 2, 3 or 4, wherein said effective rate is at least about 18.0 kGy/hour.

13. The method according to claim 1, 2, 3 or 4, wherein said effective rate is at least about 30.0 kGy/hour.

14. The method according to claim 1, 2, 3 or 4, wherein said effective rate is at least about 45 kGy/hour.

15. The method according to claim 1, 2, 3 or 4, wherein said one or more tissues is maintained in a low oxygen atmosphere.

16. The method according to claim 1, 2, 3 or 4, wherein said one or more tissues is maintained in an atmosphere comprising at least one noble gas or nitrogen.

17. The method according to claim 16, wherein said noble gas is argon.

18. The method according to claim 1, 2, 3 or 4, wherein said one or more tissues is treated prior to irradiation with at least one cycle of being subjected to a vacuum and then being placed under an atmosphere comprising at least one noble gas or nitrogen.

19. The method according to claim 2, 3 or 4, wherein said residual solvent content is reduced by a method selected from the group consisting of lyophilization, drying, concentration, addition of a second solvent, evaporation, chemical extraction, spray-drying and vitrification.

20. The method according to claim 2, 3 or 4, wherein said residual solvent content is less than about 15%.

21. The method according to claim 2, 3 or 4, wherein said residual solvent content is less than about 10%.

22. The method according to claim 2, 3 or 4, wherein said residual solvent content is less than about 3%.

23. The method according to claim 2, 3 or 4, wherein said residual solvent content is less than about 2%.

24. The method according to claim 2, 3 or 4, wherein said residual solvent content is less than about 1%.

25. The method according to claim 2, 3 or 4, wherein said residual solvent content is less than about 0.5%.

26. The method according to claim 2, 3 or 4, wherein said residual solvent content is less than about 0.08%.

27. The method according to claim 1, 2, 3 or 4, wherein at least one sensitizer is added to said one or more tissues prior to said step of irradiating said one or more tissues.

28. The method according to claim 1, 2, 3, or 4, wherein said one or more tissues contains at least one biological contaminant or pathogen selected from the group consisting of viruses, bacteria, yeasts, molds, fungi, parasites and prions or similar agents responsible, alone or in combination, for TSEs.

29. The method according to claim 2, 3 or 4, wherein said at least one stabilizer is an antioxidant.

30. The method according to claim 2, 3 or 4, wherein said at least one stabilizer is a free radical scavenger or spin trap.

31. The method according to claim 2, 3 or 4, wherein said at least one stabilizer is a combination stabilizer.

32. The method according to claim 2, 3 or 4, wherein said at least one stabilizer is a ligand.

33. The method according to claim 32, wherein said ligand is heparin.

34. The method according to claim 2, 3 or 4, wherein said at least one stabilizer reduces damage due to reactive oxygen species.

35. The method according to claim 2, 3 or 4, wherein said at least one stabilizer is selected from the group consisting of: ascorbic acid or a salt or ester thereof; glutathione; vitamin E or a derivative thereof, including Trolox; albumin; sucrose; glycylglycine; L-carnosine; cysteine; silymarin; diosmin; hydroquinonesulfonic acid; 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; uric acid or a salt or ester thereof; methionine; histidine; N-acetyl cysteine; lipoic acid; sodium formaldehyde sulfoxylate; gallic acid or a derivative thereof; propyl gallate; ethanol; acetone; rutin; epicatechin; biacalein; purpurogallin; coumaric acid; deferoxamine; ergothionine; thiourea; trehalose; polylysine; dimethylurea; mercaptoethylamine; dimethyl-2-thiourea and mixtures of two or more thereof.

36. The method according to claim 35, wherein said mixtures of two or more stabilizers are selected from the group consisting of: mixtures of ethanol and acetone; mixtures of ascorbic acid, or a salt or ester thereof, and uric acid, or a salt or ester thereof; mixtures of ascorbic acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, and albumin; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, albumin and sucrose; mixtures of ascorbic acid, or a salt or ester thereof, and glycylglycine; mixtures of ascorbic acid, or a salt or ester thereof, glycylglycine and albumin; mixtures of ascorbic acid, or a salt or ester thereof, and L-carnosine; mixtures of ascorbic acid, or a salt or ester thereof, and cysteine; mixtures of ascorbic acid, or a salt or ester thereof, and N-acetyl cysteine; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, and silymarin; mixtures of ascorbic acid, or a salt or ester

thereof, uric acid, or a salt or ester thereof, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, and diosmin; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and lipoic acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and hydroquinonesulfonic acid; mixtures of Trolox, α-lipoic acid, coumaric acid and n-propyl gallate;and mixtures of uric acid, or a salt or ester thereof, lipoic acid, sodium formaldehyde sulfoxylate, gallic acid, or a derivative thereof, propyl gallate, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid.

37. The method according to claim 2, 3 or 4, wherein said at least one stabilizer is a dipeptide stabilizer.

38. The method according to claim 37, wherein said dipeptide stabilizer is selected from the group consisting of glycyl-glycine (Gly-Gly), carnosine and anserine.

39. The method according to claim 1, 2, 3 or 4, wherein said radiation is corpuscular radiation, electromagnetic radiation, or a mixture thereof.

40. The method according to claim 39, wherein said electromagnetic radiation is selected from the group consisting of radio waves, microwaves, visible and invisible light, ultraviolet light, x-ray radiation, gamma radiation and combinations thereof.

41. The method according to claim 1, 2, 3 or 4, wherein said radiation is gamma radiation.

42. The method according to claim 1, 2, 3 or 4, wherein said radiation is E-beam radiation.

43. The method according to claim 1, 2, 3 or 4, wherein said radiation is visible light.

44. The method according to claim 1, 2, 3 or 4, wherein said radiation is ultraviolet light.

45. The method according to claim 1, 2, 3 or 4, wherein said radiation is x-ray radiation.

46. The method according to claim 1, 2, 3 or 4, wherein said radiation is polychromatic visible light.

47. The method according to claim 1, 2, 3 or 4, wherein said radiation is infrared.

48. The method according to claim 1, 2, 3 or 4, wherein said radiation is a combination of one or more wavelengths of visible and ultraviolet light.

49. The method according to claim 1, 2, 3 or 4, wherein said irradiation is conducted at ambient temperature.

50. The method according to claim 1, 2, 3 or 4, wherein said irradiation is conducted at a temperature below ambient temperature.

51. The method according to claim 1, 2, 3 or 4, wherein said irradiation is conducted below the freezing point of at least one or more solvents within or surrounding said one or more tissues.

52. The method according to claim 1, 2, 3 or 4, wherein said irradiation is conducted below the eutectic point of at least one or more solvents within or surrounding said one or more tissues.

53. The method according to claim 1, 2, 3 or 4, wherein said irradiation is conducted at a temperature above ambient temperature.

54. A composition comprising one or more tissues and at least one stabilizer in an amount effective to preserve said one or more tissues for their intended use following sterilization with radiation.

55. A composition comprising one or more tissues, wherein the residual solvent content of said one or more tissues is at a level effective to preserve said one or more tissues for their intended use following sterilization with radiation.

56. The composition of claim 55, wherein said residual solvent content is less than about 15%.

57. The composition of claim 55, wherein said residual solvent content is less than about 10%.

58. The composition of claim 55, wherein said residual solvent content is less than about 5%.

59. The composition of claim 55, wherein said residual solvent content is less than about 2%.

60. The composition of claim 55, wherein said residual solvent content is less than about 1%.

61. The composition of claim 55, wherein said residual solvent content is less than about 0.5%.

62. The composition of claim 55, wherein said residual solvent content is less than about 0.08%.

63. The composition of claim 54 or 55, wherein said one or more tissues is glassy or vitrified.

64. The method according to claim 2, 3 or 4, wherein said non-aqueous solvent is selected from the group consisting of glycerol, DMSO, ethanol, acetone, PPG, and mixtures thereof.

65. The method according to claim 64, wherein said PPG is PPG 400, PPG 1200 or PPG 2000.

66. The method according to claim 2, 3 or 4, wherein said residual solvent content is about 0%.

67. The method according to claim 2, 3 or 4, wherein said residual solvent content is about 1%.

68. The method according to claim 2, 3 or 4, wherein said residual solvent content is about 2.4%.

69. The method according to claim 2, 3 or 4, wherein said residual solvent content is about 4.8%.

70. The method according to claim 2, 3 or 4, wherein said residual solvent content is about 7%.

71. The method according to claim 2, 3 or 4, wherein said residual solvent content is about 9%.

72. The method according to claim 2, 3 or 4, wherein said residual solvent content is about 10%.

73. The method according to claim 2, 3 or 4, wherein said residual solvent content is about 20%.

74. The method according to claim 2, 3 or 4, wherein said residual solvent content is about 33%.

75. The composition of claim 54, wherein said at least one stabilizer is selected from the group consisting of: ascorbic acid or a salt or ester thereof; glutathione; vitamin E or a derivative thereof; albumin; Trolox; coumaric acid; sucrose; glycylglycine; L-carnosine; cysteine; silymarin; diosmin; hydroquinonesulfonic acid; 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; uric acid or a salt or ester thereof; methionine; histidine; N-acetyl cysteine; lipoic acid; sodium formaldehyde sulfoxylate; gallic acid or a derivative thereof; propyl gallate; ethanol; acetone; rutin; epicatechin; biacalein; purpurogallin; coumaric acid; deferoxamine; ergothionine; thiourea; trehalose; polylysine; dimethylurea; mercaptoethylamine; dimethyl-2-thiourea and mixtures of two or more thereof.

76. The composition according to claim 75, wherein said mixtures of two or more stabilizers are selected from the group consisting of: mixtures of ethanol and acetone; mixtures of ascorbic acid, or a salt or ester thereof, and uric acid, or a salt or ester thereof; mixtures of ascorbic acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic

acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, and albumin; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, albumin and sucrose; mixtures of ascorbic acid, or a salt or ester thereof, and glycylglycine; mixtures of ascorbic acid, or a salt or ester thereof, glycylglycine and albumin; mixtures of ascorbic acid, or a salt or ester thereof, and L-carnosine; mixtures of ascorbic acid, or a salt or ester thereof, and cysteine; mixtures of ascorbic acid, or a salt or ester thereof, and N-acetyl cysteine; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, and silymarin; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, and diosmin; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and lipoic acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and hydroquinonesulfonic acid; mixtures of Trolox, α-lipoic acid, and coumaric acid; mixtures of Trolox, α-lipoic acid, coumaric acid and n-propyl gallate; and mixtures of uric acid, or a salt or ester thereof, lipoic acid, sodium formaldehyde sulfoxylate, gallic acid, or a derivative thereof, propyl gallate, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid.

77. A method for prophylaxis or treatment of a condition or disease or malfunction of a tissue in a mammal comprising introducing into a mammal in need thereof one or more tissues sterilized according to a method according to claim 1, 2, 3 or 4.

78. The method according to claim 2, 3 or 4, wherein said residual solvent is an aqueous solvent.

79. The method according to claim 2, 3 or 4, wherein said one or more tissues is suspended in said solvent.

80. The method according to claim 1, 2, 3 or 4, wherein said irradiation is conducted below the glass transition point of at least one or more solvents within or surrounding said one or more tissues.

81. The method according to claim 1, 2, 3 or 4, wherein the recovery of the desired characteristic(s) of said one or more tissues after sterilization by irradiation is greater than 100% of the pre-irradiation value.

82. The method according to claim 1, 2, 3 or 4, wherein the recovery of the desired characteristic(s) of said one or more tissues after sterilization by irradiation is at least about 100% of the pre-irradiation value.

83. The method according to claim 1, 2, 3 or 4, wherein the recovery of the desired characteristic(s) of said one or more tissues after sterilization by irradiation is at least about 90% of the pre-irradiation value.

84. The method according to claim 1, 2, 3 or 4, wherein the recovery of the desired characteristic(s) of said one or more tissues after sterilization by irradiation is at least about 80% of the pre-irradiation value.

85. The method according to claim 1, 2, 3 or 4, wherein the recovery of the desired characteristic(s) of said one or more tissues after sterilization by irradiation is at least about 70% of the pre-irradiation value.

86. The method according to claim 1, 2, 3 or 4, wherein the recovery of the desired characteristic(s) of said one or more tissues after sterilization by irradiation is at least about 60% of the pre-irradiation value.

87. The method according to claim 1, 2, 3 or 4, wherein the recovery of the desired characteristic(s) of said one or more tissues after sterilization by irradiation is at least about 50% of the pre-irradiation value.

88. A composition comprising one or more tissues prepared according to a method of one of claims 1, 2, 3 or 4.

89. The method according to claim 2, 3 or 4, wherein said residual solvent content is less than about 80%.

90. The method according to claim 2, 3 or 4, wherein said residual solvent content is less than about 50%.

91. The composition of claim 55, wherein said residual solvent content is less than about 80%.

92. The composition of claim 55, wherein said residual solvent content is less than about 50%.

93. A composition comprising one or more tissues, at least one non-aqueous solvent and at least one stabilizer, wherein said non-aqueous solvent and said stabilizer are present in a combined amount effective to preserve said one or more tissues for their intended use following sterilization with radiation.

94. The composition of claim 93, wherein said at least one non-aqueous solvent comprises DMSO and said at least one stabilizer comprises ascorbate.

95. The composition of claim 93, wherein said at least one non-aqueous solvent comprises DMSO and said at least one stabilizer comprises a mixture of ascorbate, coumaric acid and n-propyl gallate.

96. The composition of claim 93, wherein said at least one non-aqueous solvent comprises PPG and said at least one stabilizer comprises ascorbate.

97. The method according to claim 4, wherein, said at least two stabilizing processes comprise:

a. adding to said one or more tissues at least one stabilizer; and
b. adding to said one or more tissues at least one non-aqueous solvent.

98. The method according to claim 97, wherein said at least one non-aqueous solvent comprises DMSO and said at least one stabilizer comprises ascorbate.

99. The method according to claim 97, wherein said at least one non-aqueous solvent comprises DMSO and said at least one stabilizer comprises a mixture of ascorbate, coumaric acid and n-propyl gallate.

100. The method according to claim 97, wherein said at least one non-aqueous solvent comprises PPG and said at least one stabilizer comprises ascorbate.

101. The method according to claim 2, 3 or 4, wherein the residual solvent is a mixture of an organic solvent and an aqueous solvent.

102. A composition comprising one or more tissues and at least one stabilizer, wherein the residual solvent content of said one or more tissues is at a level that together with said at least one stabilizer is effective to preserve said one or more tissues for their intended use following sterilization with radiation.

103. The composition according to claim 54, 55 or 102, wherein the oxygen content of said one or more tissues is reduced to a level that together with said at least one stabilizer and/or said residual solvent content is effective to protect said one or more tissues from sterilization with radiation.

104. The composition according to claim 88, wherein said one or more tissues is selected from the group consisting of heart valves, ligaments and demineralized bone matrix.

105. The method according to claim 2, 3 or 4, wherein said step of adding to said one or more tissues at least one stabilizer comprises at least one method selected from the group consisting of: soaking the tissue in a solution containing said at least one stabilizer, optionally under pressure, at elevated temperature and/or in the presence of a penetration enhancer; applying a gas containing said at least one stabilizer, optionally under pressure and/or at elevated temperature; injecting said at least one stabilizer or a solution containing said at least one stabilizer directly into said tissue; placing said tissue under reduced pressure and then introducing a gas or solution at a higher pressure containing said at least one stabilizer; dehydrating said tissue and rehydrating said tissue with a solution containing said at least one stabilizer; applying a high ionic strength solvent containing said at least one stabilizer, optionally followed by a controlled reduction in the ionic strength of said solvent; cycling said

tissue between solutions of high ionic and/or osmolar strength and solutions of low ionic and/or osmolar strength containing said at least one stabilizer; and combinations of two or more thereof.

106. The method according to claim 2, 3 or 4, wherein said step of adding to said one or more tissues at least one stabilizer further comprises adding at least one compound effective to increase penetration of said at least one stabilizer into said tissue.

107. An assay for determining the optimal conditions for sterilizing a tissue that contains collagen without adversely affective a predetermined biological characteristic or property thereof, said method comprising the steps of: (i) irradiating collagen under a pre-determined set of conditions effective to sterilize said tissue ; (ii) determining the turbidity of said irradiated collagen; and (iii) repeating steps (i) and (ii) with a different pre-determined set of conditions until said turbidity of said irradiated collagen reaches a pre-determined acceptable level.

108. The method according to claims 1, 2, 3 or 4, wherein said step of irradiating said one or more tissues produces substantially no neo-antigens therein.

109. The method according to claims 1, 2, 3 or 4, wherein said step of irradiating said one or more tissues reduces the number of reactive allo-antigens and/or xeno-antigens.

110. A composition comprising one or more tissues and at least one stabilizer, wherein the residual solvent content of said one or more tissues is at a level which, together with the amount of said at least one stabilizer, is effective to preserve said one or more tissues for their intended use following sterilization with radiation.

111. The method according to claim 18, wherein said one or more tissues is treated prior to irradiation with at least three cycles of being subjected to a vacuum and then being placed under an atmosphere comprising at least one noble gas or nitrogen.

112. The method according to claim 77, wherein the production of negative characteristics in said one or more tissues following introduction into said mammal is insufficient to render said one or more tissues unsafe and/or ineffective for the intended use thereof.

113. The method according to claim 77, wherein the amount of negative characteristics in said one or more tissues following introduction into said mammal is less than about 0.5%.

114. The method according to claim 77, wherein the amount of negative characteristics in said one or more tissues following introduction into said mammal is less than about 1%.

115. The method according to claim 77, wherein the amount of negative characteristics in said one or more tissues following introduction into said mammal is less than about 2%.

116. The method according to claim 77, wherein the amount of negative characteristics in said one or more tissues following introduction into said mammal is less than about 5%.

117. The method according to claim 77, wherein the amount of negative characteristics in said one or more tissues following introduction into said mammal is less than about 10%.

118. The method according to claim 112, wherein said negative characteristic is selected from the group consisting of inflammation and calcification.

119. The method according to claim 118, wherein said one or more tissues comprises at least one heart valve.

120. The method according to claim 1, 2, 3 or 4, wherein said one or more tissues are packaged prior to said irradiation.

121. The method according to claim 106, wherein said at least one compound effective to increase penetration of said at least one stabilizer into said tissue is selected from the group consisting of compounds that cause an increase in the distance between molecules in the tissue and compounds that cause macromolecules in the tissue to become less compact, or relaxed.

122. The method according to claim 106, wherein said at least one compound effective to increase penetration of said at least one stabilizer into said tissue is cationic when said at least one stabilizer is anionic.

123. The method according to claim 106, wherein said at least one compound effective to increase penetration of said at least one stabilizer into said tissue is anionic when said at least one stabilizer is cationic.